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Stephen Richmond

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EXAMINER

BOWERS, NATHAN ANDREW

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/631,845	Applicant(s) RICHMOND ET AL.	
	Examiner NATHAN A. BOWERS	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 and 33-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 10-16, 20-22, 33-35 and 38-42 is/are allowed.
- 6) ☒ Claim(s) 1-9, 17-19, 36 and 37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Objections

Claim 36 is objected to because of the following informalities: it is understood that the claim should read “between about 0.1 mm and about 4.0 mm” rather than “between about 0.1 and about 40 mm.” There is no support in the specification for 40 mm as an endpoint. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1, 2, 5, 6, 18, 19, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) in view of Bullen (US 20030132109).

With respect to claim 1, Magnuson discloses a method for the automated picking of animal cell colonies. This is disclosed in paragraph [0015]. Paragraphs [0068], [0119]-[0130], and [0178] teach that a picking head comprising a hollow pin (Figure 3) is moveable about the apparatus using positioning motors. A dispensing container and a sample container including a plurality of animal cell colonies held in a medium are placed onto the apparatus according to paragraphs [0117] and [0132]. Magnuson discloses in paragraphs [0015] and [0059] that the dispensing container comprises an array of wells separated by a characteristic spacing. Paragraph [0068] states that machine vision and image processing features are used to identify animal cell colony locations in the sample container, and the picking head is moved to above the sample container in response. Specifically, paragraphs [0018] and [0074] disclose a camera as a useful image capturing device, and paragraphs [0099]-[0102] disclose image processing software. Paragraph [0069] and [0117] teach that the hollow pin is aligned with the animal cell colony locations, and that a distal end of the hollow pin is introduced into the cell medium proximate to the animal cell colony by an offset distance. Cells are aspirated into the hollow pin and expelled into the dispensing container through the movement of the picking head.

Magnuson, however, does not expressly state that the inside diameter of the hollow pin is greater than the diameter of the animal cell colonies.

Bullen discloses a hollow pin pipette (Figure 8:20) used to select a desired cell (Figure 8:62) or cell colony from a well (Figure 8:122). Cells are aspirated into the interior of the pipette, and are transported to different wells (Figure 8:124,126) where they are subjected to various tests. This is described in paragraph [0046]. It is apparent from the Figure that the diameter of the pipette is larger than the diameter of the collected cell (62). Paragraph [0045] states that inner diameter of the pipette is approximately 1.28 mm, which is larger than the average cell colony (~0.5 mm).

Magnuson and Bullen are analogous art because they are from the same field of endeavor regarding the collection and transportation of cells using a suction device.

At the time of the invention, it would have been obvious to increase the diameter of the hollow pin disclosed by Magnuson so that it is larger than the diameter of the individual cell colonies to be collected. Although a larger hollow tube diameter would make it harder to produce a seal upon contact with the cell colonies, the increased size would be beneficial because it would allow one to aspirate greater cell quantities at a time, thus improving the efficiency of collection. As evidenced by Bullen, pipetting tools of at least 0.5 mm in diameter are known in the art as common instruments capable of collecting desired cells from a large cell population.

With respect to claim 2, Magnuson and Bullen disclose the method in claim 1. Magnuson additionally teaches that the picking step comprises repeating the aligning and

aspirating steps for the hollow pin in order to pick multiple ones of the animal cell colonies. This is taught in paragraph [0059].

With respect to claims 5 and 6, Magnuson and Bullen disclose the method in claim 1. In addition, Magnuson teaches that the animal cell colonies are stained either with a contrast enhancing agent or a fluorescent agent to assist the imaging processing. In paragraph [0111], Magnuson teaches that dark field microscopy and fluorescence-assisted detection can be employed in the invention.

With respect to claims 18 and 19, Magnuson and Bullen disclose the method in claim 1. In addition, Magnuson teaches that the animal cell colony comprises either a plurality of cells or a single cell. Paragraphs [0116]-[0118] teach that the invention may be used to process a plurality of cells or a single cell.

With respect to claims 36 and 37, Magnuson discloses the method in claim 1. Magnuson, further teaches that the offset distance between the distal end of the pin and the base of the container is dictated by the vertical height of the adherent animal cell colony. Accordingly, if colonies with heights of 0.25 to 1.0 mm are present, then the offset distance between the pin and the base during collection will be 0.25 to 1.0 mm.

2) Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) and Bullen (US 20030132109) as applied to claim 1, and further in view of Bienert (US 20010019845).

Magnuson and Bullen disclose the method set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however, do not expressly disclose a plurality of hollow pins are used in the collection of animal cells.

Bienert discloses a picking head comprising a plurality of pins capable of automatically transporting biological cells from a sample container to a dispensing container. This is taught in paragraphs [0035]-[0045] and generally throughout the reference. Pins are selectively moved into a transfer position and simultaneously or independently activated in order to collect samples in parallel. It is apparent from Figure 2 that Bienert's invention is capable of aligning with the characteristic spacing of a well plate array.

Magnuson and Bienert are analogous art because they are from the same field of endeavor regarding the automatic collection and dispersion of biological samples.

At the time of the invention, it would have been obvious to ensure that the invention disclosed by Magnuson contained a plurality of hollow pins each individually aligned with the characteristic spacing of the wells located in the dispensing container. The simultaneous processing of a plurality of samples in parallel is advantageous because the sampling process can be accomplished more quickly with better accuracy. The use of multiple hollow tubes correlating to multiple wells reduces cross contamination since different tubes are used to collect different samples. The process can be easily automated to enhance reproducibility.

3) Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) and Bullen (US 20030132109) as applied to claim 1, and further in view of Sogi (US 4210724).

Magnuson discloses the method set forth in claims 1 and 10 as set forth in the 35 U.S.C. 102 rejection above. In addition, Magnuson discloses in paragraphs [0011] and [0020] that the animal cell colonies are adhered to the sample container and immersed in a medium. Magnuson, however, does not expressly disclose that the distal end of the pin is agitated relative to the sample container so as to produce turbulence in the medium to detach the animal cell colony at the location prior to performing the aspirating step. Magnuson does not disclose a drive mechanism for causing lateral or rotary motion of the distal ends of the pins to facilitate detachment of animal cell colonies.

Sogi discloses an apparatus for automatically transporting cells in a culturing solution to a dispensing container by collecting the desired cells in a pipette through suction. This is taught in the abstract and in column 10, line 54 to column 11, line 48. Column 11, line 49 to column 13, line 16 teach that a drive mechanism is provided to cause the tip of the pipette to quickly oscillate in the culture solution during collection in order to facilitate detachment of cell colonies adhered to the sample container. The pipette is intrinsically capable of performing both lateral and rotary oscillations.

Magnuson and Sogi are analogous art because they are from the same field of endeavor regarding the automatic collection and transportation of cultured cells.

At the time of the invention, it would have been obvious to provide Magnuson's invention with a drive mechanism capable of oscillating the distal ends of the pins in order to facilitate, during collection, the detachment of animal cell colonies adhered to the sample container. Sogi teaches in column 3, lines 36-40 and column 13, lines 33-42 that automatic agitation of the culture solution is a highly efficient way to ensure that the cells are suspended in

the sample and fully gather during the collection process. Magnuson teaches in paragraph [0011] that animal cells are characterized by a high affinity for the surfaces upon which they are immobilized during growth. In this way, agitation and scraping forces would have been necessary to dislodge the adherent cells from their growth substrates. Therefore, it would have been obvious to use the distal ends of the tips to dislodge the target cells by producing turbulence in the medium.

4) Claims 4, 7-9 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) and Bullen (US 20030132109) as applied to claim 1, and further in view of Parekh (US 6064754).

With respect to claim 4, Magnuson and Bullen disclose the method set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. In addition, Magnuson discloses in paragraphs [0011] and [0020] that the animal cell colonies are adhered to the sample container and immersed in a medium. Magnuson, however, does not expressly disclose that the distal end of the pin is agitated relative to the sample container so as to produce turbulence in the medium to detach the animal cell colony at the location prior to performing the aspirating step.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 7, lines 13-20 state that proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55 indicate that an automated picking apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis. Column 13, line 56 to column 14, line 7 teaches that the tips of the picking apparatus are agitated relative to the

sample container in order to collect the target material. This agitation intrinsically must produce turbulence in the medium.

Magnuson and Parekh are analogous art because they are from the same field of endeavor regarding the automatic imaging, collection, and dispensing of biological components.

At the time of the invention, it would have been obvious to agitate the distal ends of the pins located in the picking apparatus disclosed by Magnuson. Magnuson teaches in paragraph [0011] that animal cells are characterized by a high affinity for the surfaces upon which they are immobilized during growth. In this way, agitation and scraping forces would have been necessary to dislodge the adherent cells from their growth substrates. Therefore, it would have been obvious to use the distal ends of the tips to dislodge the target cells through direct contact or by producing turbulence in the medium.

With respect to claims 7-9, Magnuson discloses the method set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however does not expressly disclose that the plurality of animal cell colonies comprise or express a biological molecule of interest, namely biopharmaceutical proteins.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 2, lines 8-20 and column 4, lines 20-51 teach that the biological material may comprise biopharmaceutical proteins expressed from a cell culture. Column 7, lines 13-20 state that the proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55 indicate that an automated picking

apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis.

At the time of the invention, it would have been obvious to use Magnuson's invention to selectively aspirate and dispense animal cells that express biological molecules, and, more specifically, biopharmaceutical proteins. In column 2, lines 8-20, Parekh teaches that the presence, absence, or altered expression of many different proteins can be associated with a disease or a condition of interest. Studying the expression of these products using Magnuson's device would therefore been advantageous in order to better understand physiological problems associated with difficulties in gene expression. Furthermore, biomolecules are often useful as therapeutic agents, and as markers for diagnosis, prognosis, and evaluating response to treatment. Therefore, it would have been beneficial to develop methods designed to detect, isolate, and consolidate animal cells that express biopharmaceutical proteins in order to produce a cell product that has valuable medicinal or therapeutic applications.

With respect to claim 17, Magnuson discloses the method set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however does not expressly disclose that the animal cell colonies are held suspended in the medium.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 7, lines 13-20 state that proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55 indicate that an automated picking apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis. Column 2, lines

21-49 teach that the target biological materials are suspended in a semi-solid gel prior to collection by the picking apparatus.

At the time of the invention, it would have been obvious to suspend the animal cells disclosed by Magnuson in a semi-solid gel rather than allowing the cells to adhere to the sample container. In column 6, lines 2-12, Parekh teaches that gels are capable of suspending biological materials prior to collection, and are non-interfering with respect to fluorescence detection and image processing. Applicant teaches on page 1 of the specification that mammalian cell colonies held in suspension in a semi-solid medium are well known in the art.

Allowable Subject Matter

Claims 10-16, 20-22, 33-35 and 38-42 are allowed.

With respect to independent claim 10, the prior art does not disclose, in the claimed environment, an apparatus for picking animal cell colonies that comprises at least one hollow pin including an inner pin and an outer pin such that the inner pin is recessed axially inside the outer pin. Clearly, Magnuson does not disclose the use of multiple concentrically arranged pins. Bullen and Hoummady (US 20070025880) disclose the use of an inner pin recessed axially inside the end of an outer pin. In each reference, however, sample quantities are not aspirated into the inner pin.

Response to Arguments

Applicant's arguments filed 17 April 2008 with respect to the 35 U.S.C. 112 rejections have been fully considered and are persuasive. Therefore, these rejections have been withdrawn.

However, upon further consideration, a new ground of rejection is made in view of the combination of Magnuson with Bullen.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/William H. Beisner/
Primary Examiner, Art Unit 1797

/Nathan A Bowers/
Examiner, Art Unit 1797